Tetrahedron Letters,Vol.24,No.42,pp 4499-4502,1983 0040-4039/83 $3.00 + .00
Printed in Great Britain

SOME UNUSUAL REACTIONS OF MOLECULAR OXYGEN WITH BICYCLIC DIAZENES WHICH TYPICALLY SERVE AS PRECURSORS TO ALKYLIDENECYCLOPENTANE-1,3-DIYLS; PEROXIDE FORMATION [1]

R. Daniel Little,*[2] Lorraine Losinski-Dang, Manuel G.
Venegas, & Craig Merlic [3]

Department of Chemistry University of
California, Santa Barbara Santa Barbara, California 93106

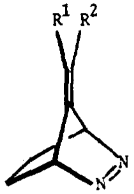
Abstract

The reaction of a series of substituted bicyclic diazenes with oxygen was investigated. Three types of products result, namely ketoalcohols **2b–f**, ketoaldehydes **4e–g** and dioxolanes **3e–g.** The potential intermediacy of an endoperoxide **5f** is considered.

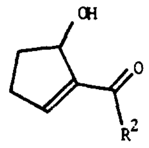
In 1979, we reported that the linearly fused tricyclopentanoid ring system which is common to a number of biologically active natural products, could be simply and efficiently prepared through utilization of the intermolecular 1,3-diyl trapping reaction.[4] For example, simply refluxing a solution of the dimethyldiazene **1a** in the presence of an excess of cyclopentenone and acetonitrile as the solvent, led to the formation of a regio- and stereochemical mixture of three tricyclopentanoids in 90-98% isolated yield. In marked contrast with this result was the discovery that repetition of this experiment using the **p**-methoxyphenyldiazene **1b** in place of compound **1a** afforded a meager 24-30% yield of the desired ring system along with an appreciable contribution to the product mixture in terms of the formation of both bridged cycloadducts (34-43%) and diyl dimer (remainder of the material).

Using the dimethyl diyl derived from diazene **1a,** Berson and coworkers have demonstrated that the fused cycloadducts arise primarily by way of a reaction between the singlet diyl and a diylophile, while the bridged cycloadducts arise mainly from a reaction of the triplet diyl. When the trapping reaction is conducted in the presence of molecular oxygen, which selectively scavenges the triplet diyl, the ratio of the fused to bridged cycloadducts reflects the ratio for capture of pure singlet diyl.[5]

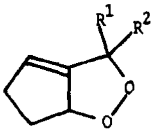
In analogy with these experiments, and in an effort to selectively scavenge the triplet diyl derived from the **p**-methoxyphenyldiazene **1b**, a mixture of **1b** and a large excess (eighty-seven fold) of cyclopentenone was refluxed in acetonitrile while a steady stream of molecular oxygen was bubbled through the solution. To our surprise, neither fused nor bridged cycloadducts were formed. Instead, the crystalline ketoalcohol **2b**, formally corresponding to the product resulting from a combination of the diyl and oxygen, was isolated in 75% yield. The same result was obtained when the reactive diylophile dimethylfumarate was used in place of cyclopentenone. Thus, unlike the results obtained from the reaction of the dimethyl diyl in the presence of both molecular oxygen and dimethylfumarate, the **p**-methoxyphenyl diyl undergoes preferential reaction with oxygen.[6]



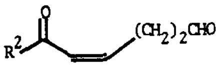
1a-h



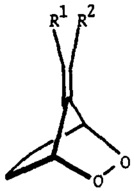
2b-g



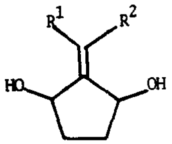
3a, **3h**,
3e-g



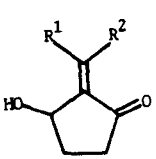
4e-g



5f



6f



7f

$\underline{a}$, $R^1 = R^2 = CH_3$
$\underline{b}$, $R^1 = H$, $R^2 = \underline{p}\text{-}CH_3OC_6H_4$
$\underline{c}$, $R^1 = H$, $R^2 = \underline{p}\text{-}ClC_6H_4$
$\underline{d}$, $R^1 = H$, $R^2 = C_6H_5$
$\underline{e}$, $R^1 = H$, $R^2 = CH_3$
$\underline{f}$, $R^1 = H$, $R^2 = C(CH_3)_2$
$\underline{g}$, $R^1 = H$, R^2 = cyclohexyl
$\underline{h}$, $R^1 = R^2 = C_6H_5$

To explore the generality of this transformation, diazenes **1c–g** were prepared and each in turn was refluxed in acetonitrile in the presence of a stream of oxygen. Like the **p**-methoxyphenyl system **1b**, the **p**-chlorophenyl and phenyl diazenes **1c** and **1d** each afforded ketoalcohols **2c** and **2d** in 75 and 50% yields, respectively. The monoalkyl substituted system **1e–g** provided differing results in that, in addition to the formation of ketoalcohols **2e–g**, two other products corresponding to dioxolanes **3e–g** and ketoaldehyde **4e–g**, were also produced.[7] It is of interest to note that Wilson and Geiser have also reported the isolation of dioxolanes **3a** and **3h** in 37% and 40% yields as a result of heating diazenes **1a** and **1h** to 40°C in the presence of 80-150 psi of oxygen.[8]

In the present instance, dioxolanes **3e–g** exhibited reasonably "high" thermal stability.[9] For example, less than 5% of dioxolane **3e** was converted to ketoalcohol **2e** after refluxing a solution of **3e** in acetonitrile for 3h, both in the presence and absence of oxygen.[10] In contrast, thermolysis of diazene **1e** in the presence of oxygen afforded approximately 25% of **2e** after the same time period.

The potential intermediacy of the bridged peroxide **5** was examined. Endoperoxide **5f** was conveniently prepared from isopropylfulvene following the methodology developed by Adam and coworkers.[11] It's structure was firmly established by spectroscopic and wet chemical methods. Thus, treatment of **5f** with thiourea (MeOH, 0°C) led to the formation of diol **6f** while treatment with triethylamine (CH_2Cl_2, 0°C) afforded ketoalcohol **7f**. However, under no set of conditions which we have utilized thus far have we been able to observe the conversion of the endoperoxide to any one of the compounds **2e**, **3e**, or **4e**. This result probably should not be construed as providing conclusive evidence which rules out the intermediacy of the endoperoxide, since if it is formed from any one of the diazenes, it's decomposition could be influenced by factors inherent to the diazene reaction conditions including, for example, the presence of singlet and/or triplet diyl as well as unreacted diazene and perhaps, singlet or triplet oxygen.[12] Clearly additional experiments designed to probe in greater detail the pathway(s) which lead to products **2–4** are in order. The results of these studies will be published in due course.

Acknowledgements. We are pleased to acknowledge support of this research by the National

Institutes of Health (grant number CA 21144) and the Alfred P. Sloan Foundation.

References and Notes

1. Presented by LLD at the Second Chemical Congress of the North American Continent, Las Vegas, Nevada, August 1980.

2. Alfred. P. Sloan Foundation Fellow, 1980-1984.

3. NSF Undergraduate Research Program Participant.

4. Little, R. D.; Bukhari, A.; Venegas, M. G. Tetrahedron Lett. 1979, 305-309.

5. (a) Berson, J. A. Acc. Chem. Res. 1968, 4, 466. (b) Berson, J. A. "Capturable Diradicals of the Trimethylenemethane Series" in Diradicals, Borden, W. T., Ed. Wiley, New York, 1982, pp. 151-194.

6. We do not mean to suggest the reaction sequence necessarily involves a reaction between an alkylidenecyclopentane-1,3-diyl and oxygen. Another possibility, for example, involves the reaction of oxygen with the diyl formed after the cleavage of one C-N bond rather than two.

7. The product composition varied as a function of the rate of addition of oxygen. We have not yet explored this point in detail. For an example of a reaction wherein the product composition from a photochemically induced extrusion of nitrogen from a diazene is dependent upon the oxygen content of the sample see: Turro, N. J.; Renner, G. A.; Waddell, W. H.; Katz, T. J. J. Am. Chem. Soc. 1976, 98, 4320.

8. Wilson, R. N.; Geiser, F. J. Am. Chem. Soc. 1978, 100, 2225.

9. Adam and coworkers have reported that the structurally similar molecule 4-ethylidene-3,3,5,5-tetramethyl-1,2-dioxolane is thermally quite stable and undergoes a reaction at 315°C. Adam, W.; Arce, J. J. Am. Chem. Soc. 1975, 97, 926.

10. We were unable to detect the presence of ketoaldehyde **4e**.

11. (a) Adam, W.; Bloodworth, A. J. Topics in Current Chemistry, Boschke, F. L. Ed. Springer-Verlag, New York, pp. 121-158. (b) Balci, M. Chem. Reviews, 1981, 81, 91-108 and refs. therein. (c) Adam, W.; Erden, I. Angew. Chem. Int. Ed. Engl. 1978, 17, 210; Adam, W.; Eggelte, H. J. J. Org. Chem. 1977, 42, 3978.

12. (a) Salomon, R. G.; Salomon, M. F. J. Am. Chem. Soc. 1977, 99, 3501. (b) Zagorski, M. G.; Salomon, R. G. Ibid. 1980, 102, 2501.

(Received in USA 1 June 1983)